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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,345	11/14/2003	Rosana Kapeller-Libermann	MPI00-418P1RDV1M	5860

7590 10/19/2006

MILLENNIUM PHARMACEUTICALS, INC.
75 Sidney Street
Cambridge, MA 02139

EXAMINER	
HOWARD, ZACHARY C	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/713,345	KAPELLER-LIBERMANN, ROSANA	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/24/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Alignment #1*.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The preliminary amendment of 11/14/03 has been entered in full. Claims 1-20 are canceled. New claims 21-33 are added.

Claims 21-33 are under consideration in the instant application.

Specification

The disclosure is objected to because of the following informalities:

(1) The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "ANTIBODY THAT BINDS 47174, A NOVEL HUMAN GLYCOSYLTRANSFERASE".

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 21, 23, 25, 29, 31 and 33 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

These claims, as written, do not sufficiently distinguish over cells that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" as taught in the Abstract of the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody, or portion thereof, that specifically binds to the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for an antibody, or portion thereof, that binds to a fragment of SEQ ID NO: 2 having glycosyltransferase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is an antibody, or portion thereof, that specifically binds to the amino acid sequence of SEQ ID NO: 2 or a fragment thereof having glycosyltransferase activity. Applicants have given the protein of SEQ ID NO: 2 the designation "47174". Applicants teach the cloning of 47174 cDNA (Example 1); the tissue distribution of 47174 mRNA (highest expression in brain tissues; see Examples 2 and 3 and Table 1) and recombinant expression of the 47174 protein in bacterial and COS cells (Example 4 and 5). Applicants teach, based on sequence similarity, that the protein is a glycosyltransferase ("A search was performed against the HMM database resulting in the identification of a "glycosyltransferase" domain in the amino acid sequence of human 47174 at about residues 154 to 336 of SEQ ID NO:2"; pg 5, ¶ 68).

Applicants provide an alignment between SEQ ID NO: 1 and a consensus amino acid sequence of a glycosyltransferase group 2 domain (Figure 2). Applicants do not provide a working example of glycosyltransferase activity for the protein, or teach a glycosylated substrate for the protein.

Toba (2000) teaches a human GalNAc-T9 protein that is 99.7% similar to instant SEQ ID NO: 2 (see Figure 1 of Toba et al, Biochimica et Biophysica 1493: 264-268, published September 7th, 2000; cited as reference AR on the 2/24/2004 IDS). Each protein is 603 amino acids; an alignment of the two sequences is attached to this Office Action as Sequence Alignment #1. There are two mismatches between the sequences (positions 235 and 351); the remaining residues are identical. Toba further teaches brain-specific expression of the mRNA encoding the GalNAc-T9 protein. Toba tests a substrate for the protein but does not identify a substrate; "[t]he soluble enzyme in the medium, however, did not glycosylated apo-mucin prepared from bovine submaxillary glands (data not shown). Judging from the restricted expression of GalNAc-T9 in the brain, it may catalyze brain-specific O-glycosylation...[a]n assay using synthetic peptides including sequences of these [brain-specific] proteins may help detect the activity of GalNAc-T9 (see pg 267-268).

The relevant art teaches the high level of difficulty in identifying substrates of GalNAc polypeptide transferases (also known as ppGalNAcT). Hang (2005) teaches, "the precise roles of the ppGalNActTs in mucin-type O-linked glycosylation have been elusive due to their lack of primary consensus sequence in their protein substrates. Consequently, identification of the physiological substrates for each of the ppGalNAcT isoforms has been extremely challenging" (Hang et al, 2005, Bioorganic & Medicinal Chemistry, 13: 5021-5034). Furthermore, the Examiner can find no reports that have identified the substrate of the GalNAc-T9 taught by Toba.

The claims are directed to antibodies to fragments of SEQ ID NO: 2 having glycosyltransferase activity. The genus of molecules including fragments of SEQ ID NO: 2 includes any sequence consisting of two or more contiguous amino acids selected from SEQ ID NO: 2. Given that SEQ ID NO: 2 is 603 amino acids in length, this genus encompasses an extremely large number of fragments. The claims are directed to those

fragments that have "glycosyltransferase activity". However, the specification does not teach where in the sequence of SEQ ID NO: 2 that amino acids can be deleted and retain activity, nor does the specification provide a working example of a fragment of SEQ ID NO: 2 with glycosyltransferase activity.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. Although the specification outlines art-recognized procedures for producing fragments, this is not adequate guidance as to the nature of active fragments that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, it may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore deletion of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39; Doerks *et al.* (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics **15**(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in sequence databases but watch out for the traps." Trends in Genetics **12**(10): 425-427].

It is acknowledged that the level of skill of those in the art is high, but it is not disclosed and not predictable from the limited teachings of the prior art and specification which fragments of SEQ ID NO: 2 have glycosyltransferase activity. There are no examples of fragments of SEQ ID NO: 2 have glycosyltransferase activity. Thus the specification fails to teach the skilled artisan how to make and use antibodies to a genus of fragments with glycosyltransferase activity without resorting to undue

experimentation. The specification has not provided the person of ordinary skill in the art the guidance necessary to be able to make and use the antibodies to a genus of fragments with glycosyltransferase activity.

Due to the large quantity of experimentation necessary to (1) identify a substrate of SEQ ID NO: 2 for testing glycosyltransferase activity and (2) generate and screen for activity the large number of fragments recited in the claims, the lack of guidance presented in the specification regarding which amino acids are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 21-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicants are claiming and what Applicants have possession of.

The claims are genus claims because the claims are directed to antibodies to variant polypeptides. The genus is highly variant because a significant number of structural differences between the variant polypeptides are permitted. The claims encompass antibodies to any fragment of SEQ ID NO: 2 (as small as two contiguous amino acids) that has glycosyltransferase activity. Thus, the claims are drawn to antibodies to a genus of polypeptides defined only by sequence similarity. However, the instant specification fails to describe the entire genus of polypeptides that are

encompassed by each of these claims. From the specification, it is clear that Applicants have possession of antibodies to an isolated polypeptide of SEQ ID NO: 2. The specification fails to describe or teach any other polypeptide which differs from the sequence of SEQ ID NO: 2 and which has a glycosyltransferase activity. The claims, however, are not limited to antibodies to a polypeptide of SEQ ID NO: 2.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of the genus of polypeptide fragments to which the antibodies are generated. There is not even identification of any particular portion of the structure that must be conserved. Structural features that could distinguish encoded polypeptides in the genus from others in the protein class are missing from the disclosure. The specification and claims do not provide any description of what changes should be made. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of

species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an antibody, or portion thereof, that specifically binds to the amino acid sequence of SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicants are reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see pg 1115).

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "specifically" in claims 21 and 31 is a relative term which renders each claim indefinite. The term "specifically" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The degree of binding of the antibody to SEQ ID NO: 2 is rendered indefinite by the use of the term "specifically". This specification does not clarify whether or not an antibody that specifically binds to SEQ ID NO: 2 can bind to another polypeptide or not. Does specific binding limit that the antibody to one that binds to SEQ ID NO: 2 but does not bind to any other polypeptides? Or does the term include antibodies that bind to SEQ ID NO: 2 with a greater specificity than to other polypeptides. If so, neither the specification nor the claims clarify what degree of binding is sufficient to meet the limit of "specifically binds". For purposes of prosecution, the claim has been interpreted broadly to encompass any antibody that binds to SEQ ID NO: 2.

The remaining claims are rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-23, 26-28 and 30-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toba et al (Biochimica et Biophysica 1493: 264-268, published September 7th, 2000; cited as reference AR on the 2/24/2004 IDS) in view of Clausen et al (U.S. Patent Number 5,871,990, published 2/16/1999).

Toba teaches a GalNAc-T9 protein that consists of 603 amino acids (see Figure 1). This protein is 99.7% similar to instant SEQ ID NO: 2; an alignment of the two sequences is attached to this Office Action as Sequence Alignment #1. There are two mismatches between the two sequences at positions 235 and 351; the remainder of the positions are identical. Toba does not teach antibodies to this protein.

Clausen teaches a GalNAc-T3 protein. Clausen further teaches antibodies to said protein, including polyclonal antibodies, monoclonal antibodies, chimeric antibodies, F(ab) fragments, F(ab')2 fragments, and labeled antibodies (column 12, lines 22-67). Clausen further teaches that said antibodies "can be used as reagents for the detection and purification of GalNAc-T3" (column 12, lines 20-21).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to make antibodies as taught by Clausen for use with the GalNAc-T9 protein as taught by Toba. The person of ordinary skill in the art would be motivated to do so because in order to purify the GalNAc-T9 protein taught by Toba for enzymatic assays, or to perform immunohistochemistry to determine the tissue expression of the protein. Further, a person of ordinary skill in the art would have a reasonable expectation of success because Toba teaches the sequence of the GalNAc-T9 protein, and Clausen teaches antibody techniques. Further, due to the high degree of similarity between the GalNAc-T9 protein taught by Toba and instant SEQ ID NO: 1 (601 of 603 amino acids are identical), including numerous regions of 20 or more amino acids that are identical, numerous antibodies that would bind to the GalNAc-T9 protein taught by Toba would also bind to instant SEQ ID NO: 1.

Claims 24, 25 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toba et al (Biochimica et Biophysica 1493: 264-268, published September 7th, 2000; cited as reference AR on the 2/24/2004 IDS) in view of Clausen et al (U.S. Patent Number 5,871,990, published 2/16/1999) as applied to claim 21 above, and in further view of Sandhu et al (1992. Critical Reviews in Biotechnology. 12(5/6): 437-462).

The teachings of Toba and Clausen are summarized above. Clausen further teaches, "The antibodies may be elicited in an animal host by immunization with

GalNAc-T3 components or may be formed by in vitro immunization of immune cells" (column 12, lines 24-26). Neither reference specifically teaches humanized, human or murine antibodies.

Sandhu teaches murine monoclonal antibodies, human monoclonal antibodies, and humanized monoclonal antibodies (see pg 437). Sandhu teaches that "hybridoma technology has made it feasible to prepare large quantities of monoclonal antibodies (MAb) with a defined antigen specificity" (pg 437). Sandhu teaches murine antibodies, human antibodies, and humanized antibodies (pg 437). Sandhu further teaches, "humanization of murine MAbs is a technique that is now applied widely to MAbs" (pg 446).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to make antibodies as taught by Clausen for use with the GalNAc-T9 protein as taught by Toba, and further to make the antibodies murine, human or humanized as taught by Sandhu. The person of ordinary skill in the art would be motivated to do so because in order to purify the GalNAc-T9 protein taught by Toba for enzymatic assays, or to perform immunohistochemistry to determine the tissue expression of the protein, and because Clausen does not teach the specific species of antibody (i.e., murine, human, humanized, etc) to use, one of skill in the art would turn to the relevant teachings in the art, such as Sandhu. Further, a person of ordinary skill in the art would have a reasonable expectation of success because Toba teaches the sequence of the GalNAc-T9 protein, Clausen teaches that antibody techniques, and Sandhu teaches that murine, human and humanized antibodies are routine in the art. Further, due to the high degree of similarity between the GalNAc-T9 protein taught by Toba and instant SEQ ID NO: 1 (601 of 603 amino acids are identical), including numerous regions of 20 or more amino acids that are identical, numerous murine, human or humanized antibodies that would bind to the GalNAc-T9 protein taught by Toba would also bind to instant SEQ ID NO: 1.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

zch

GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

SEQUENCE ALIGNMENT

#1

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RESULT 1
GALT9_HUMAN
ID   GALT9_HUMAN    STANDARD;      PRT;   603 AA.
AC   Q9HCQ5; Q6NT54; Q8NFR1;
DT   16-AUG-2004, integrated into UniProtKB/Swiss-Prot.
DT   16-AUG-2004, sequence version 2.
DT   07-FEB-2006, entry version 28.
DE   Polypeptide N-acetylgalactosaminyltransferase 9 (EC 2.4.1.41)
DE   (Protein-UDP acetylgalactosaminyltransferase 9) (UDP-
DE   GalNAc:polypeptide N-acetylgalactosaminyltransferase 9) (Polypeptide
DE   GalNAc transferase 9) (GalNAc-T9) (pp-GaNTase 9).
GN   Name=GALNT9;
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC   Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1), AND TISSUE SPECIFICITY.
RC   TISSUE=Brain;
RX   MEDLINE=20435310; PubMed=10978536; DOI=10.1016/S0167-4781(00)00180-9;
RA   Toba S., Tenno M., Konishi M., Mikami T., Itoh N., Kurosaka A.;
RT   "Brain-specific expression of a novel human UDP-GalNAc:polypeptide N-
RT   acetylgalactosaminyltransferase (GalNAc-T9).";
RL   Biochim. Biophys. Acta 1493:264-268(2000).
RN   [2]
RP   NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 2).
RC   TISSUE=Kidney;
RA   Guo J.H., Zan Q., Yu L.;
RL   Submitted (DEC-2001) to the EMBL/GenBank/DDBJ databases.
RN   [3]
RP   ENZYME ACTIVITY.
RX   MEDLINE=22393469; PubMed=12407114; DOI=10.1074/jbc.M203094200;
RA   Zhang Y., Iwasaki H., Wang H., Kudo T., Kalka T.B., Hennet T.,
RA   Kubota T., Cheng L., Inaba N., Gotoh M., Togayachi A., Guo J.-M.,
RA   Hisatomi H., Nakajima K., Nishihara S., Nakamura M., Marth J.D.,
RA   Narimatsu H.;
RT   "Cloning and characterization of a new human UDP-N-acetyl-alpha-D-
RT   galactosamine:polypeptide N-acetylgalactosaminyltransferase,
RT   designated pp-GalNAc-T13, that is specifically expressed in neurons
RT   and synthesizes GalNAc alpha-serine/threonine antigen.";
RL   J. Biol. Chem. 278:573-584(2003).
CC   -!- FUNCTION: Catalyzes the initial reaction in O-linked
CC       oligosaccharide biosynthesis, the transfer of an N-acetyl-D-
CC       galactosamine residue to a serine or threonine residue on the
CC       protein receptor. Does not glycosylate apomucin or SDC3.
CC   -!- CATALYTIC ACTIVITY: UDP-N-acetyl-D-galactosamine + polypeptide =
CC       UDP + N-acetyl-D-galactosaminyl-polypeptide.
CC   -!- COFACTOR: Manganese and calcium (By similarity).
CC   -!- PATHWAY: Glycosylation.
CC   -!- SUBCELLULAR LOCATION: Golgi apparatus; Golgi membrane; single-pass
CC       type II membrane protein (By similarity).
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC       Name=1;
CC         IsoId=Q9HCQ5-1; Sequence=Displayed;
CC       Name=2;
CC         IsoId=Q9HCQ5-2; Sequence=VSP_011206;
CC         Note=No experimental confirmation available;
CC   -!- TISSUE SPECIFICITY: Specifically expressed in brain. Not expressed
CC       in heart, placenta, lung, liver, skeletal muscle, kidney,
CC       pancreas, spleen, thymus, prostate, testis, ovary, small
CC       intestine, colon and leukocyte. In brain, it is expressed in
CC       cerebellum, frontal lobe, temporal lobe, putamen and spinal cord,
CC       weakly expressed in cerebral cortex. Not expressed in medulla and
CC       occipital pole.
CC   -!- DOMAIN: There are two conserved domains in the glycosyltransferase
CC       region: the N-terminal domain (domain A, also called GT1 motif),
CC       which is probably involved in manganese coordination and substrate
CC       binding and the C-terminal domain (domain B, also called
CC       Gal/GalNAc-T motif), which is probably involved in catalytic
CC       reaction and UDP-Gal binding (By similarity).
CC   -!- DOMAIN: The ricin B-type lectin domain binds to GalNAc and
CC       contributes to the glycopeptide specificity (By similarity).
CC   -!- SIMILARITY: Belongs to the glycosyltransferase 2 family. GalNAc-T
CC       subfamily.
CC   -!- SIMILARITY: Contains 1 ricin B-type lectin domain.
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   EMBL; AB040672; BAB13699.2; -; mRNA.
DR   EMBL; AF458594; AAM49722.1; -; mRNA.
DR   Ensembl; ENSG00000182870; Homo sapiens.
DR   HGNC; HGNC:4131; GALNT9.
DR   MIM; 606251; gene.
DR   GO; GO:0016020; C:membrane; NAS.
DR   GO; GO:0004653; F:polypeptide N-acetylgalactosaminyltransfera. . .; NAS.
DR   GO; GO:0006493; P:protein amino acid O-linked glycosylation; NAS.
DR   InterPro; IPR001173; Glyco_trans_2.
DR   InterPro; IPR000772; Ricin_B_lectin.
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DR   Pfam; PF00535; Glycos_transf_2; 1.
DR   Pfam; PF00652; Ricin_B_lectin; 1.
DR   SMART; SM00458; RICIN; 1.
DR   PROSITE; PS50231; RICIN_B_LECTIN; 1.
KW   Alternative splicing; Calcium; Glycoprotein; Glycosyltransferase;
KW   Golgi stack; Lectin; Manganese; Membrane; Signal-anchor; Transferase;
KW   Transmembrane.
FT   CHAIN         1    603       Polypeptide N-
FT                                acetylgalactosaminyltransferase 9.
FT                                /FTId=PRO_0000059120.
FT   TOPO_DOM      1      6       Cytoplasmic (Potential).
FT   TRANSMEM      7     29       Signal-anchor for type II membrane
FT                                protein (Potential).
FT   TOPO_DOM     30    603       Lumenal (Potential).
FT   DOMAIN      464    600       Ricin B-type lectin.
FT   REGION      150    261       Catalytic subdomain A.
FT   REGION      318    380       Catalytic subdomain B.
FT   CARBOHYD    460    460       N-linked (GlcNAc. . .) (Potential).
FT   DISULFID    477    493       By similarity.
FT   DISULFID    525    540       By similarity.
FT   DISULFID    567    587       By similarity.
FT   VARSPLIC      1    366       Missing (in isoform 2).
FT                                /FTId=VSP_011206.
FT   CONFLICT    235    235       T -> A (in Ref. 1).
FT   CONFLICT    299    299       W -> R (in Ref. 1).
FT   CONFLICT    351    351       D -> G (in Ref. 1).
FT   CONFLICT    539    539       K -> R (in Ref. 1).
SQ   SEQUENCE   603 AA;  68477 MW;  5A46EBA9FF3862CD CRC64;

  Query Match             99.7%;  Score 3179;  DB 1;  Length 603;
  Best Local Similarity   99.7%;  Pred. No. 1.8e-246;
  Matches  601;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 MAVARKIRTLLTVNILVFVGIVLFSVYCRLQGRSQELVRIVSGDRRVRSRHAKVGTLGDR 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MAVARKIRTLLTVNILVFVGIVLFSVYCRLQGRSQELVRIVSGDRRVRSRHAKVGTLGDR 60

Qy         61 EAILQRLDHLEEVVYNQLNGLAKPIGLVEGPGGLGQGGLAATLRDDGQEAEGKYEEYGYN 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 EAILQRLDHLEEVVYNQLNGLAKPIGLVEGPGGLGQGGLAATLRDDGQEAEGKYEEYGYN 120

Qy        121 AQLSDRISLDRSIPDYRPRKCRQMSYAQDLPQVSVVFIFVNEALSVILRSVHSVVNHTPS 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 AQLSDRISLDRSIPDYRPRKCRQMSYAQDLPQVSVVFIFVNEALSVILRSVHSVVNHTPS 180

Qy        181 QLLKEVILVDDNSDNVELKFNLDQYVNKRYPGLVKIVRNSRREGLIRARLQGWKAATAPV 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||| |||||
Db        181 QLLKEVILVDDNSDNVELKFNLDQYVNKRYPGLVKIVRNSRREGLIRARLQGWKTATAPV 240

Qy        241 VGFFDAHVEFNTGWAEPALSRIREDRRRIVLPAIDNIKYSTFEVQQYANAAHGYNWGLWC 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 VGFFDAHVEFNTGWAEPALSRIREDRRRIVLPAIDNIKYSTFEVQQYANAAHGYNWGLWC 300

Qy        301 MYIIPPQDWLDRGDESAPIRTPAMIGCSFVVDREYFGDIGLLDPGMEVYGGENVELGMRV 360
              |||||||||||||||||||||||||||||||||||||||||||||||| ||||||||
Db        301 MYIIPPQDWLDRGDESAPIRTPAMIGCSFVVDREYFGDIGLLDPGMEVYGDENVELGMRV 360

Qy        361 WQCGGSMEVLPCSRVAHIERTRKPYNNDIDYYAKRNALRAAEVWMDDFKSHVYMAWNIPM 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 WQCGGSMEVLPCSRVAHIERTRKPYNNDIDYYAKRNALRAAEVWMDDFKSHVYMAWNIPM 420

Qy        421 SNPGVDFGDVSERLALRQRLKCRSFKWYLENVYPEMRVYNNTLTYGEVRNSKASAYCLDQ 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 SNPGVDFGDVSERLALRQRLKCRSFKWYLENVYPEMRVYNNTLTYGEVRNSKASAYCLDQ 480

Qy        481 GAEDGDRAILYPCHGMSSQLVRYSADGLLQLGPLGSTAFLPDSKCLVDDGTGRMPTLKKC 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 GAEDGDRAILYPCHGMSSQLVRYSADGLLQLGPLGSTAFLPDSKCLVDDGTGRMPTLKKC 540

Qy        541 EDVARPTQRLWDFTQSGPIVSRATGRCLEVEMSKDANFGLRLVVQRCSGQKWMIRNWIKH 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 EDVARPTQRLWDFTQSGPIVSRATGRCLEVEMSKDANFGLRLVVQRCSGQKWMIRNWIKH 600

Qy        601 ARH 603
              |||
Db        601 ARH 603
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